CLAIM AMENDMENTS

1-18. (canceled)

19. (currently amended): A method to prepare a desired polyketide which method comprises incubating required substrates with ~~the polyketide synthase of claim 6~~ a hybrid modular polyketide synthase (PKS) comprising at least a first extender module and a second extender module of a different PKS from said first module,

wherein said extender modules are defined as consisting of the amino acid sequence from the N-terminus of the ketosynthase (KS) domain through the C-terminus of the acyl transferase protein (ACP) domain;

wherein the C-terminus of said first module is covalently linked to the N-terminus of a intra-molecular linker (RAL) and the N-terminus of the second module is covalently linked to the C-terminus of said RAL, and

wherein said RAL is defined as the amino acid sequence between the C-terminus of an upstream ACP domain and the N-terminus of an adjacent downstream KS domain; said ACP and KS domains occupying adjacent modules in the same reading frame;

wherein either said first module or second module is not covalently linked to said RAL in a naturally occurring polyketide synthase;

whereby the RAL effects the transfer of a nascent polyketide chain from said first module to said second module.

20. (original): The method of claim 19 wherein the substrates comprise a diketide thioester and thioesters of the required extender units.

21. (original): The method of claim 20 wherein the extender units are malonyl, methylmalonyl, ethylmalonyl or hydroxymalonyl thioesters.

22. (canceled)

23. (new): The method of claim 19 wherein said first and second extender modules have structures that are present in naturally occurring PKS.

24. (new): The method of claim 19 wherein said RAL is selected from the group consisting of M2 *ery*, M4 *ery*, M6 *ery*, M2 *rif*, M3 *rif*, M5 *rif*, M3 *rap*, M4 *rap,* and M7 *rap* intra-module linkers (SEQ. ID. NO's: 3-11, respectively).

25. (new): The method of claim 19 which contains *ery* modules 1 and 3 through 6 inclusive and tylosin module 2, and wherein said polyketide chain is transferred from *ery* module 1 to *tyl* module 2 and then to *ery* modules 3 through 6 inclusive, or

which contains *ery* modules 1 through 5 inclusive and narbomycin module 6, wherein said polyketide chain is transferred from *ery* modules 1 through 5 inclusive to *nar* module 6, or

which contains modules 1 and 3 through 6 inclusive of *ery* and modules 2-3 of tylosin, spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* module 1 to modules 2-3 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive, or

which contains modules 1 through 3 inclusive of tylosin, spiramycin or niddamycin and modules 3 through 6 inclusive of *ery*, and wherein said polyketide chain is transferred from modules 1 through 3 inclusive of said tylosin, spiramycin or niddamycin to *ery* modules 3 through 6 inclusive, or

which contains a module of tylosin, spiramycin or niddamycin and modules 1-2 and 3 through 6 inclusive of *ery*, wherein said polyketide chain is transferred from *ery* modules 1-2 to the tylosin, spiramycin or niddamycin module and then to *ery* modules 3 through 6 inclusive, or

which contains modules 1 and 3 through 6 inclusive of *ery* and module 5 of tylosin, spiramycin or niddamycin.having the enoyl reductase catalytic activity inactivated, wherein said polyketide chain is transferred from *ery* module 1 to module 5 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive, or

which contains *ery* modules 1 through 4 inclusive and 6 and module 6 of spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* modules 1 through 4 inclusive to module 6 of spiramycin or niddamycin and then to *ery* module 6, or

which contains module 1 of FK-506 or 520 and modules 2 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of FK-506 or 520 and then to modules 2 through 14 inclusive of rapamycin, or

which contains module 1 and 11 through 14 inclusive of rapamycin and modules 2 through 6 inclusive of FK-506 or 520 wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 6 inclusive of FK-506 or 520 and then to modules 11 through 14 inclusive of rapamycin, or

which contains module 1 of rapamycin, modules 2 through 7 inclusive of FK-506 or 520 and modules 12 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 7 inclusive of FK-506 or 520 and then to modules 12 through 14 inclusive of rapamycin, or

which contains module 1 of rapamycin, modules 2 through 8 inclusive of FK-506 or 520 and modules 13-14 of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 8 inclusive of FK-506 or 520 and then to modules 13-14 of rapamycin, or

which contains modules 1 through 10 inclusive of rapamycin and modules 7 through 10 inclusive of FK-506 or 520, wherein said polyketide chain is transferred from modules 1 through 10 inclusive of rapamycin to modules 7 through 10 inclusive of FK-506 or 520.

26. (new): A method to prepare a desired polyketide which method comprises incubating required substrates with a hybrid modular polyketide synthase (PKS) comprising at least a first extender module and a second extender module of a different PKS from said first module,

wherein said extender modules are defined as consisting of the amino acid sequence from the N-terminus of the ketosynthase (KS) domain through the C-terminus of the acyl transferase protein (ACP) domain;

wherein the C-terminus of said first module is covalently linked to the N-terminus of a inter-molecular linker (ERL) and the N-terminus of the second module is covalently linked to the C-terminus of said ERL, and

wherein said ERL is defined as a contiguous polypeptide comprising, in order, (1) the amino acid sequence beginning at the C-terminus of the ACP domain of the most downstream module of a

first open reading frame and (2) the amino acid sequence upstream of the N-terminus of the most upstream KS domain of a second open reading frame, which second open reading frame is immediately adjacent to and downstream of said first open reading frame; and

wherein either said first module or second module is not covalently linked to said ERL in a naturally occurring polyketide synthase;

whereby the ERL effects the transfer of a nascent polyketide chain from said first module to said second module.

27. (new): The method of claim 26 wherein the substrates comprise a diketide thioester and thioesters of the required extender units.

28. (new): The method of claim 27 wherein the extender units are malonyl, methylmalonyl, ethylmalonyl or hydroxymalonyl thioesters.

29. (new): The method of claim 26 wherein said first and second extender modules have structures that are present in naturally occurring PKS.

30. (new): The method of claim 26 wherein the portion of the ERL at the N-terminus of the second module is selected from the group consisting of SEQ. ID. NO's: 12-19, respectively.

31. (new): The method of claim 26 which contains *ery* modules 1 and 3 through 6 inclusive and tylosin module 2, and wherein said polyketide chain is transferred from *ery* module 1 to *tyl* module 2 and then to *ery* modules 3 through 6 inclusive, or

which contains *ery* modules 1 through 5 inclusive and narbomycin module 6, wherein said polyketide chain is transferred from *ery* modules 1 through 5 inclusive to *nar* module 6, or

which contains modules 1 and 3 through 6 inclusive of *ery* and modules 2-3 of tylosin, spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* module 1 to modules 2-3 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive, or

which contains modules 1 through 3 inclusive of tylosin, spiramycin or niddamycin and modules 3 through 6 inclusive of *ery*, and wherein said polyketide chain is transferred from

modules 1 through 3 inclusive of said tylosin, spiramycin or niddamycin to *ery* modules 3 through 6 inclusive, or

which contains a module of tylosin, spiramycin or niddamycin and modules 1-2 and 3 through 6 inclusive of *ery*, wherein said polyketide chain is transferred from *ery* modules 1-2 to the tylosin, spiramycin or niddamycin module and then to *ery* modules 3 through 6 inclusive, or

which contains modules 1 and 3 through 6 inclusive of *ery* and module 5 of tylosin, spiramycin or niddamycin having the enoyl reductase catalytic activity inactivated, wherein said polyketide chain is transferred from *ery* module 1 to module 5 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive, or

which contains *ery* modules 1 through 4 inclusive and 6 and module 6 of spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* modules 1 through 4 inclusive to module 6 of spiramycin or niddamycin and then to *ery* module 6, or

which contains module 1 of FK-506 or 520 and modules 2 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of FK-506 or 520 and then to modules 2 through 14 inclusive of rapamycin, or

which contains module 1 and 11 through 14 inclusive of rapamycin and modules 2 through 6 inclusive of FK-506 or 520 wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 6 inclusive of FK-506 or 520 and then to modules 11 through 14 inclusive of rapamycin, or

which contains module 1 of rapamycin, modules 2 through 7 inclusive of FK-506 or 520 and modules 12 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 7 inclusive of FK-506 or 520 and then to modules 12 through 14 inclusive of rapamycin, or

which contains module 1 of rapamycin, modules 2 through 8 inclusive of FK-506 or 520 and modules 13-14 of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 8 inclusive of FK-506 or 520 and then to modules 13-14 of rapamycin, or

which contains modules 1 through 10 inclusive of rapamycin and modules 7 through 10 inclusive of FK-506 or 520, wherein said polyketide chain is transferred from modules 1 through 10 inclusive of rapamycin to modules 7 through 10 inclusive of FK-506 or 520.